

Ankylosing Spondylitis

Also called: Rheumatoid spondylitis

Ankylosing spondylitis is a type of arthritis of the spine. It causes swelling between your vertebrae, which are the disks that make up your spine, and in the joints between your spine and pelvis. Ankylosing spondylitis is an autoimmune disease. This means your immune system, which normally protects your body from infection, attacks your body's own tissues. The disease is more common and more severe in men. It often runs in families.

Early symptoms include back pain and stiffness. These problems often start in late adolescence or early adulthood. Over time, ankylosing spondylitis can fuse your vertebrae together, limiting movement. Symptoms can worsen or improve or stop altogether. The disease has no cure, but medicines can relieve the pain, swelling and other symptoms. Exercise can also help.

National Institute of Arthritis and Musculoskeletal and Skin Disease

Ankylosing Spondylitis Genes Found

Work supported by the National Institute of Arthritis and Musculoskeletal Skin Diseases has led to the discovery of two genes responsible for ankylosing spondylitis (AS), an inflammatory and potentially disabling disease of the spine.

The discovery of the two genes - ARTS1 and IL23R - brings the scientific community closer to fully understanding AS, says John D. Reveille, M.D., professor and director of the Division of Rheumatology and Clinical Immunogenetics at the University of Texas (UT) Medical School at Houston, who led the study with Matthew A. Brown, M.D., professor of immunogenetics at Australia's University of Queensland.

In earlier studies of identical twins, Dr. Brown and his colleagues found that the cause of ankylosing spondylitis is more than 90 percent genetic. With the discovery of the newly identified genes, a large proportion of the genetic risk for AS has now been identified.

The IL23R gene, says Dr. Brown, plays a role in the immune system's response to infection. ARTS1 is involved in processing infectious agents into "bite-size chunks" that can be seen - and fought - by the body's immune system.

The recent discovery is based on work from the largest and most comprehensive genome-wide association scan conducted to date. In this part of the research project, investigators were searching for genetic information related to AS, as well as autoimmune thyroid disease/Graves' Disease, breast cancer and multiple sclerosis.

"This discovery, to me, is the most important since 1973, when HLA-B27 was discovered," says Reveille colleague Frank C. Arnett, M.D., professor of internal medicine and pathology and laboratory medicine at the UT Medical School. HLA-B27 is a powerful predisposing gene that increases the risk of getting AS by more than 100 times.

Dr. Arnett says the location of the genes and the fact they don't coincide with those of autoimmune diseases, such as rheumatoid arthritis, lupus or juvenile diabetes, helps refute the long-held notion that AS is an autoimmune disease. "It is looking more like AS is not an autoimmune disease, but really an unusual response to infection. These genes working together probably impair the immune system's ability to rid the body of some of these bacteria or their products."

He also believes this discovery could eventually lead to ways to immunize people against AS. "I think these give us the genetic handles to identify the pathways that are involved in AS. Once you know the dysregulated pathway, you can find a drug to either strengthen or inhibit the pathway."

In the meantime, Dr. Reveille says the two genes, along with HLA-B27, could also help physicians identify patients who are at the highest risk for developing AS. "For example, if you have a family member with AS, a simple blood test would be able to tell us if you are also at risk," he says. "We could offer screenings for people with inflammatory back pain. In the past, [testing for the HLA-B27 gene] was all we had. Now we potentially have more tests."

"This is a success story for genetics work," says Dr. Reveille. "I think it will lead the way for other work to be done."

AS is a chronic inflammatory arthritis characterized by joint stiffness, pain and extra bone growth that can result in partial or complete fusion of the spine. It typically strikes adolescent and young adult males. Currently there is no cure for the disease.

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Wellcome Trust Case Control Consortium and the Australo-Anglo-American Spondylitis Consortium. Association scan of 14,500 nonsynonymous SNPs in four diseases identifies autoimmunity variants. *Nature Genetics* 2007; 39 :1329-1337.

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